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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,073	12/07/2001	Anthony M. Jevnikar	024916-011	8806

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EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/005,073

Applicant(s)

JEVNIKAR ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/12/04.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 52-101 is/are pending in the application.
- 4a) Of the above claim(s) 53-58,62,64-68,92-94 and 96-101 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 52,59-61,63,69-91 and 95 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendments and 1.132 declarations of Inventor Jevnikar filed 7/12/04 are acknowledged.
2. Claims 53-58, 62, 64-68, 92-94, and 96-101 stand withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to nonelected species.

Claims 52, 59-61, 63, 69-91, and 95 are being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 52, 59-61, 63, 69-91, and 95 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the action mailed 2/10/04.

Applicant's arguments, filed 7/12/04, have been fully considered but they are not persuasive. Applicant argues, "Applicants have adequately disclosed the claimed invention in the specification of the present application and, in addition, have conducted experiments demonstrating that transgenic plants expressing autoantigens fed to mice induced oral immune tolerance as described in the two declarations submitted by Dr. Jevnikar, an inventor of the claimed invention, in the parent application. A copy of both declarations are attached hereto."

While the claimed inventions may be adequately disclosed, i.e., an adequate written description has been provided, the inventions have not been adequately enabled. As set forth in the rejection, in the case of tolerance induction, it has been shown repeatedly that results in mouse models do not correlate with results in humans. Whereas tolerance has been repeatedly induced in mice, the identical/equivalent methods have not worked in humans.

Regarding the Jevnikar declarations, these declarations appear to have been submitted in the parent application in response to art rejections that are not of record in the instant application. Applicant appears to want the Examiner to sift through the declarations and attached publications and find an argument for the enablement of the instant inventions.

In the context of the instant rejection, a review of the declarations shows only that the Inventor asserts unexpected results in a mouse model. The inadequacy of mouse models in the instant context has been addressed. However, the Inventor's assertion of unexpected results must be seen as an admission of the unexpected nature of the instant inventions, even in a mouse model. The Inventor cannot credibly merely assert that the unexpected results are due solely to the expression of the antigen in transgenic plants. It is just as (or more) likely that the unexpected results are due to: 1) the specific animal model, 2) the specific disease model, 3) the specific antigen, or 4) the specific transgenic plant species expressing the antigen. Given the breadth of the instant claims, i.e., the immunosuppression of any immune response to any antigen transgenically expressed in any plant, it would seem that the declarations as a whole tend to support the rejection for lack of enablement given the Inventor's own assertion that the results in a single embodiment of the claimed invention are unexpected.

Applicant argues that *in vivo* testing is not necessary to satisfy the enablement requirement.

Applicant is advised that while *in vivo* data is not required, adequate enablement is. In this case said enablement has not been provided for the reasons of record, said reasons being supported by demonstrations of the lack of efficacy and indeed, danger, of administering antigens to humans in attempts to induce tolerance.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 52, 59-61, 63, 69-91, and 95 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/07581 (1992, IDS)

in view of U.S. Patent No. 5,484,719 (IDS), for the reasons of record set forth in the action mailed 2/10/04.

Applicant's arguments, filed 7/12/04, have been fully considered but they are not persuasive. Applicant argues that the Examiner has used impermissible hindsight in the rejection.

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. So long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). It remains the Examiner's position that the combined references, in view of that which was known in the art at the time of the invention, render the instant invention obvious.

Applicant argues, that the '719 patent does not teach that mammalian antigens could be produced in transgenic plants.

The patent states, "The present invention may be used to produce any type of vaccine effective in immunizing humans and animals against disease."

Applicant argues, "the Examiner has not provided "any proof" that any immunologist would refer to induction of tolerance as the induction of a suppressive immune response".

Applicant is advised that WO 92/07581, used in the instant rejection, teaches that "the activation of helper T-cells is decreased by the induction of specific suppressor T-cells" (page 10), i.e., a teaching of tolerance as the induction of a suppressive immune response.

Applicant argues against the references individually.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by

combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings of the references to cheaply and efficiently produce the autoantigens used for the method of the instant claims.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

G.R. Ewoldt, Ph.D.
Primary Examiner
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10/5/04

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER